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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/804,490	03/12/2001	Linda Burkly	CIBT-P01-114	2374

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EXAMINER	
BRANNOCK, MICHAEL T	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/804,490	BURKLY ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *3,4,7,8,11,12,26 and 27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1,2,5,6,9,10,13-25,28 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 March 2001* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/13/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants election of Group I, claims 1, 2, 5, 6, 9, 10, 13-25, 28, 29, as the claims relate to administration of a hedgehog antagonist antibody, drawn to methods of treating cells with same, and compositions, is acknowledged. Applicant traverses the restriction requirement, stating that the subject matter of Group I (hedgehog antibodies), Group II (patched antagonists) and Group III (hedgehog antagonists) substantially overlap and thus could be examined together. This argument has been fully considered but not deemed persuasive. In the instant case, hedgehog antagonists (Group III), that were known to cause developmental abnormalities (cyclopamine), were known in the art long before the hedgehog or patched antibodies (groups I and II) reviewed in Incardona et al., Development 125(3553-3562)1998. Further Hedgehog and Patched were discovered independently of each other, and not simultaneously; additionally, their functional connection was not immediately apparent, as is well established in the art, see last paragraph of page 551 of van-den Heuvel-M et al., Nature 382(547-551)1996. Thus, although a search of any one of the groups may overlap that of another, the search of one group could not be relied upon, solely, to provide art that is anticipatory or would render obvious the invention of any other group, and to search all groups would be burdensome. Therefore, the restriction is maintained but not made final so as to allow Applicant a fair chance to respond.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 and 120 as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Drawings

The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: Figs 5A-C, The specification should refer to each part of the figures. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The replacement sheet(s) should be labeled "Replacement Sheet" in the page header (as per 37 CFR 1.84(c)) so as not to obstruct any portion of the drawing figures. If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 6, 9, 10, 18, 20-23, 28, 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the following reasons:

In claim 1, and dependent claims, set forth a goal of inhibiting growth of an epithelial cell, yet lack a step or steps that lead back to and accomplishes the recited goal; thus the claims are incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01.

Additionally, claim 1 requires an effective amount of an agent, yet does not set forth what the amount must be effective for; the specification at page 13 defines the term only by way of examples; thus the artisan could not be reasonably sure whether he or she was practicing what is claimed.

Claims 2 and 6, and dependent claims require and "antibody homolog", "homolog" being a relative term. The specification does not set forth at what point a homolog ceases to be a "anti-hedgehog antibody homolog" and only defines the term by way of examples; thus the artisan could not be reasonably sure whether he or she was practicing what is claimed.

In claim 9, the phrase "which inhibit proliferation of hair follicle keratinocytes" renders the claim indefinite because it is unclear what part of the sentence this phrase refers to.

In claim 18, it is unclear if the therapeutic composition must be suitable to accomplish the goal recited in claim 1, or that other therapeutic compositions are encompassed by the claim.

Claim 28 requires a preparation formulated for topical application to epithelial tissue, yet the specification only lists multiple ingredients that may or may not be present in such a formulation, page 28-29; thus the artisan could not tell whether a given preparation was or was not encompassed by the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 5, 9, 13-20, 24 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No: 6,639,051, Wang-EA, et al., which is fully supported by prior Application US 08/955552, filed October 20, 1997.

Wang teaches methods comprising administering hedgehog agonists to promote epithelial cell growth, including hair growth, and also methods comprising administering hedgehog antagonists to inhibit epithelial cell growth, including hair growth, see lines 10-22 of col3, lines 39-55 of col 6, lines 24-28 of col 8, lines17-28 of col 9, lines 5-14 of col 11, and topical administration see lines 65 col 11-bridging col 12, including inhibition of cutaneous epithelial keratinocytes, hair follicle stem cells and mucosal epithelial cells (see cols 9 and 10).

Claims 28 and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Ericson-J et al., Cell 87(661-673)1996.

Ericson disclose a preparation of anti-hedgehog antibodies (page 671, last column) that are indistinguishable from what the specification discloses as formulated for topical administration to epithelial cells (pages 28-29 of the instant specification), absent evidence to the contrary.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 2, 6, 10, 21-23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patent No: 6,639,051, Wang-EA, as applied to claims above 1, 5, 9, 13-20, 24, in view of Ericson-J et al., Cell 87(661-673)1996 and U.S. Patent No: 4816567.

Wang teaches methods comprising administering hedgehog agonists to promote epithelial cell growth, including hair growth, and also methods comprising administering hedgehog antagonists to inhibit epithelial cell growth, including hair growth, see lines 10-22 of col3, lines 39-55 of col 6, lines 24-28 of col 8, lines17-28 of col 9, lines 5-14 of col 11, and topical administration see lines 65 col 11-bridging col 12.

Wang does not however specifically teach that the hedgehog antagonist be an anti-hedgehog antibody. However, the use of anti-hedgehog antibodies as hedgehog antagonists was widely appreciated at the time of the filing of the Wang parent application. For example, Ericson

et al. use anti-hedgehog antibodies as hedgehog antagonists to block the generation of floor plate cells and motor neurons, see the second to the last paragraph of col 2 of page 661.

The claims also require that the anti-hedgehog antibodies be chimeric antibodies. Both Wang-EA, and Ericson-J et al. appear to be silent with respect to chimeric antibodies, however the optimization of in vivo use of antibodies by making them chimeric antibodies was well established at the time of filing the Wang parent application. U.S. Patent No: 4816567 teaches that in the art of antibody production, monoclonal antibodies are generally preferred to polyclonal antibodies (col 2, line 17), while CDR grafted and otherwise chimeric antibodies are more preferred, see col 2, lines 40-65 and cols 15 D.6 and D.7).

Therefore, it would be obvious to one of ordinary skill in the art at the time the invention was made, with reasonable expectation of success use anti-hedgehog antibodies as antagonists when practicing the method of Wang, the motivation to do so is provided by both Wang, who teaches that any hedgehog therapeutic that inhibits the activity of wild type hedgehog should be used as a matter of ordinary optimization of operating parameters (col 7, lines 41-43), and by Ericson who teach that anti-hedgehog antibodies can inhibit the activity of wild type hedgehog (col 2 of page 661), and to further routinely optimize the operation parameters, to make a chimeric, or CDR grafted antibodies according to U.S. Patent No: 4816567 when practicing the invention of Wang as modified by Ericson. The motivation to do so is provided by U.S. Patent No: 4816567 wherein in is indicated that in the art of antibody production, monoclonal antibodies are generally preferred to polyclonal antibodies (col 2, line 17), while CDR grafted and otherwise chimeric antibodies are more preferred, see col 2, lines 40-65 and cols 15 D.6 and D.7).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback, Ph.D., can be reached at (571) 272-0961.

Official papers filed by fax should be directed to (703) 872-9306. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

September 1, 2004

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER